DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

Our STN: BL 103172/5003

SEP 0 4 2001

Robert L. Garnick, Ph.D.
Genentech Incorporated
1 DNA Way
South San Francisco, CA 94080

Dear Dr. Garnick:

Your request to supplement your biologics license application for Alteplase, to provide for a 2 mg vial strength and a new indication for the restoration of function to central venous access devices (as assessed by the ability to withdraw blood) has been approved.

In accordance with approved labeling, the 2 mg vial strength will bear the trade name Cathflo Activase. The dating period for the 2 mg vials shall be 18 months from the date of manufacture when stored at 2-8°C (36-46°F). The date of manufacture shall be defined as the date of final sterile filtration of the final formulated product. Results of ongoing stability studies should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots.

The stability protocol in your supplement is considered approved for the purpose of extending the expiration dating period of your drug product as specified in 21 CFR 601.12.

We acknowledge your agreement to provide additional information and conduct postmarketing studies as described in your commitment letters of August 30, 2001, and August 31, 2001 as outlined below:

1. To evaluate the safety and efficacy of Cathflo Activase in pediatric patients, including — patients aged 2 to 16 years and — patients less than 2 years of age in an open label registry. The final protocol will be submitted to BB-IND 8569 by November 30, 2001, enrollment started by May 1, 2002, enrollment completed by April 30, 2004, and the final study report submitted to the FDA by January 2005.

2. To implement immediately the modified "trigger" temperature of 100 °F for shipping Cathflo Activase via Priority Overnight for delivery by 10:30 AM.

3. To submit by December 2001 a revised SOP "Dispensing and Shipping Commercial Drug Products (600.001)" that includes the following provisions for monitoring delivery of Cathflo Activase:

    a. To require priority delivery by 10:30 AM the next calendar day, if the outside temperature is forecast to exceed 100°F.

b. An action plan to address product disposition if product is shipped by the standard method and the actual outside temperature exceeds 100°F;

c. An action plan to address product disposition if the time of delivery exceeds the expected time (10:30 AM), under conditions in which the outside temperature exceeds 100° F; and

d. Identification of all other Genentech products that will be shipped under this revised SOP.

4. To provide periodic updates of ongoing shipping temperatures studies. The formal study protocol will be submitted to FDA by September 30, 2001, and the final study report by November 30, 2002.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

[redacted]

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 2567. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to submit draft copies of the proposed introductory advertising and promotional labeling with an FDA Form 2567 or Form 2253 to the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, HFM-602, 1401 Rockville Pike, Rockville, MD 20852-1448. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an FDA Form 2567 or Form 2253.

This information will be included in your biologics license application file.

Sincerely yours,

Glen O. Jones

for Amy Rosenberg, M.D.
Director
Division of Therapeutic Proteins
Office of Therapeutics
Research and Review
Center of Biologics
Evaluation and Research

Patricia Keegan for Dr. Weiss

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